REMARKS

This paper is in response to the Office Action dated March 13, 2006. Applicants have amended the application as set forth above. Specifically, Claims 1, 4-17 and 19-24 have been amended. New Claims 25-31 have been added. Upon entry of the amendments, Claims 1-31 remain pending in this application. No new matter is added by the amendments as discussed below. Applicants respectfully request the entry of the amendments and reconsideration of the application in view of the above amendments and the following remarks.

Submission of Priority Documents

The Examiner acknowledged Applicants' priority claims based on Korean Patent Application No. 2001-0048881 and International Patent Application No. PCT/KR02/01547. However, the Examiner noted that Applicants did not file certified copies of the priority documents. In reply, Applicants herewith submit certified copies of Korean Patent Application No. 2001-0048881 and International Patent Application No. PCT/KR02/01547. Applicants respectfully request that receipt of the priority documents be made in the next Office Action or communication.

Discussion of Amendments

The amendment to Claims 1 and 15 are made to clarify the claimed features of the subject matter and to correct grammatical errors. Support for the amendment to Claim 1 can be found in the specification, for example, at Paragraph Nos. 0010, 0020, 0022 and 0042 and in Examples 3 and 4. Support for the amendment to Claim 15 can be found, for example, Paragraph Nos. 0022, 0038-0040 and 0042. Claims 4-14, which depend from independent Claim 1, and Claims 16-19 and 22-23, which depend from independent Claim 15, have been amended to remove indefinite language and recite certain language from the related independent claims. New Claims 25-31 have been added. Support for the addition of these claims can be found, for example, in Paragraph Nos. 0010, 0020, 0022 and 0040. Claim 24 has been amended to depend from and recite certain language from Claim 26. Applicants respectfully submit that the amendments are fully supported by the application as originally filed and do not constitute the addition of new matter. Applicants respectfully request the entry of the amendments.

Discussion of Claim Objections

The Examiner objected to Claims 1-14 as including informalities, particularly the hyphen in Claim 1. In reply, Applicants have deleted the hyphen. As crossing the hyphen is not distinguishable from the hyphen itself, Applicants used brackets ([ ]) instead of crossing. Applicants respectfully submit that the pending claims do not have informalities and request the withdrawal of the objection.

Discussion of Rejection of Claims 1-24 under 35 U.S.C. §112, Second Paragraph

The Examiner rejected Claims 1-24 under Section 112, second paragraph, as being indefinite. Applicants respond to the Examiner's comments as follows:

With regard to Claims 1-14, the Examiner objected to the term "fragment" and asserted confusion over whether "fragment" referred to the fragment of the OmpF gene or to the fragment of the gene of interest. In reply, Applicants have amended Claim 1 to recite an OmpF gene encoding all or a fragment of an OmpF protein. Dependent Claim 9 has also been amended to remove the term "fragment."

With regard to Claims 15-24, the Examiner objected to the phrase "introducing the protein of interest into the vector of claim 1." In reply, Applicants have amended Claim 15 to delete the phrase.

With regard to Claim 6, the Examiner asserted confusion over the terms "gene of interest." In reply, Applicants have amended Claim 6 to recite "protein of interest" instead of "gene of interest."

Further, with regard to Claim 1, the Examiner objected to the language "said expression vector produces an OmpF fusion protein fused with the gene of interest" as unclear. The Examiner requested clarification regarding the components comprised within the fusion protein. In response, Applicants have also amended Claim 1 to recite that the fusion protein comprises an OmpF protein, a cleavage site and a protein of interest.

Discussion of Objection to the Specification

The Examiner objected to the specification under 35 U.S.C. §112, first paragraph, as failing to provide an enabling disclosure for the claimed invention. In particular, the Examiner asserted that the specification does not provide a repeatable method for obtaining the claimed expression vector pOmpF6 (accession number KCTC 1026BP), and it is not apparent if the DNA sequence is readily available to the public through deposit under the Budapest Treaty.

Applicants respectfully disagree with the Examiner and submit that the originally filed specification provides an enabling disclosure for the claimed invention. Specifically, the specification provides a repeatable process to obtain the claimed vector. See, for example, Example 3 (Development of Expression System of OmpF Gene) and Example 4 (Construction of OmpF-β-endolphin Expression Vector) at Paragraph Nos. 0030-0038.

Furthermore, Applicants respectfully submit that the expression vector pOmpF6 is readily available to the public through deposit under the Budapest Treaty. Applicants previously filed a Declaration setting forth that the subject vector was deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction of condition released to the public upon issuance of the U.S. patent. Applicants herewith resubmit a copy of the Declaration including the deposit receipt of the strain as Exhibit 1. In view of the foregoing, Applicants respectfully request the withdrawal of the objection.

Discussion of Rejection of Claims 1-24 under 35 U.S.C. §112, First Paragraph

In addition to the objection to the specification, the Examiner rejected Claims 1-24 under 35 U.S.C. §112, first paragraph for also failing to provide an enabling disclosure for the claimed invention. As previously discussed, the specification of this application provides an enabling disclosure of the claimed vector with a repeatable process to obtain the vector, and the strain at issue will be available to the public upon the issuance of the U.S. patent. Therefore, Applicants respectfully submit that the rejection of Claims 1-24 has no proper ground and request the withdrawal of the rejection.

Discussion of Rejection of Claims 1-7, 9-11, 15, 17, 18 and 20-24 under 35 U.S.C. §102(b)

The Examiner rejected Claims 1-7, 9-11, 15, 17, 18 and 20-24 under 35 U.S.C. §102(b) as being anticipated by Mizushima *et al.* (EP 0138644 B1, hereinafter "Mizushima"). The Examiner asserted that Mizushima discloses the claimed expression vector and method of producing a protein of interest. Applicants respectfully disagree with the Examiner as discussed below.

The Law of Anticipation

Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner, 778 F.2d 775 (Fed. Cir. 1985).* More particularly, a finding of anticipation requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Electro Med. Sys. S.A. v. Cooper Life Sciences, 34 F.3d 1048, 1052 (Fed. Cir. 1994).* "To anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, arranged as in the claim." *Brown v. 3M, 265 F.3d 1349 (Fed. Cir. 2001).*

Claim 1

Claim 1 is directed to an expression vector comprising an OmpF promoter, an OmpF gene encoding all or a fragment of the OmpF protein, a cleavage-site gene encoding an RNA or protein cleavage site, and a gene of interest encoding a protein of interest. The claimed expression vector is to encode a fusion protein comprising the OmpF protein, the cleavage site and the protein of interest. Further, in the expression vector the cleavage-site gene is located between the OmpF gene and the gene of interest such that the RNA or protein cleavage site is located between the OmpF protein and the protein of interest in the fusion protein.

Disclosure of Mizushima

Mizushima discloses an expression vector, which is constructed by inserting a gene coding for a useful protein into a restriction site near a promotor. Mizushima uses the term "a cleavage site" to refer to the restriction site at 3'-terminus of a specified fragment containing OmpF promoter. However, Mizushima does not teach or suggest a gene as part of the expression vector to encode a RNA or protein cleavage site in the protein obtainable from the expression vector.

Mizushima Does Not Anticipate Claim 1

In view of the foregoing, Mizushima does not teach or suggest the cleavage-site gene encoding an RNA or protein cleavage site. Also, Mizushima does not teach or suggest the fusion protein with a cleavage site expressible from the expression vector. As Mizushima does not teach all the claimed features, Mizushima does not anticipate Claim 1 and its dependent claims including Claims 2-7, 9-11, 15, 17, 18 and 20-24. Applicants respectfully request withdrawal of the rejection.

Discussion of Rejection of Claims 1-3, 6, 7, 9-11, 15, 17, 18, 22 and 24 under 35 U.S.C. §102(b)

The Examiner rejected Claims 1-3, 6, 7, 9-11, 15, 17, 18, 22 and 24 under 35 U.S.C. §102(b) as being anticipated by Nagahari *et al.* (EMBO Journal, 1985, 4/13A:3589-3592, hereinafter "Nagahari"). The Examiner asserted that Nagahari et al discloses the claimed expression vector and method of producing a protein of interest. Applicants respectfully disagree with the Examiner as discussed below.

Disclosure of Nagahari

Nagahari teaches an expression vector in which the structural gene for human β-endorphin is preceded by the OmpF gene consisting of the promoter region and the coding regions for the signal peptide and the N terminus of OmpF protein. The Nagahari expression vector encodes a fusion protein that is subjected to cleavage within the OmpF protein signal peptide region or to nonspecific protease cleavage. However, Nagahari does not teach or suggest any cleavage site located between the N terminus of OmpF protein and the β-endorphin. Nor does Nagahari teach or suggest a cleavage-site-encoding gene located between the structural gene and OmpF gene in the expression vector.

Nagahari Does Not Anticipate Claim 1

In view of the foregoing, Nagahari does not teach or suggest the cleavage-site gene located between the OmpF gene and the gene of interest. Also, Nagahari does not teach or suggest the fusion protein with a cleavage site located between the OmpF protein and the protein of interest. As Nagahari does not teach all the claimed features, Nagahari does not anticipate Claim 1 and its dependent claims including Claims 2, 3, 6, 7, 9-11, 15, 17, 18, 22 and 24. Applicants respectfully request withdrawal of the rejection.

Discussion of Rejection of Claims 1-7, 9-13, 15-18 and 20-24 under 35 U.S.C. §103(a)

The Examiner rejected Claims 1-7, 9-13, 15-18 and 20-24 under 35 U.S.C. §103(a) as being unpatentable over Mizushima taken with Simula *et al.* (Toxicology, 1993, 82/1-3:3-20, hereinafter "Simula"). Applicants respectfully disagree with the Examiner and submit that the claims are patentable over the references as discussed below.

Standard for Obviousness Rejection

The Patent and Trademark Office has the burden under section 103 to establish a *prima facie* case of obviousness. *In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-87 (Fed. Cir. 1984). To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art reference (or references when combined) must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; finally, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143.

Disclosure of Simula

Simula teaches heterologous expression of recombinant proteins via expression vectors in either *E. coli* or *Salmonella typhimurium*. Simula does not teach or suggest an expression vector comprising an OmpF gene, a gene of interest and a gene encoding an RNA or protein cleavage site and located between the OmpF gene and the gene of interest.

No *Prima Facie* Case Has Been Established

As discussed above in the anticipation rejection of claims by Mizushima, Mizushima does not teach or suggest the cleavage-site gene encoding an RNA or protein cleavage site. Also, Mizushima does not teach or suggest the fusion protein with a cleavage site expressible from the expression vector. Simula was relied on by the Examiner as a secondary reference to provide its teaching that *Salmonella* can be used as a host microorganism. Simula, however, does not remedy the deficiencies of Mizushima. As such, the combination of Mizushima and Simula does not teach or suggest all of the features of Claim 1, and therefore does not set forth a *prima facie* case of obviousness. In view of this, Applicants respectfully submit that Claim 1 and its dependent claims are patentable over the cited references in combination or alone. Withdrawal of the rejection is respectfully requested.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above.

In view of the above remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If the Examiner has any questions which may be answered by telephone, he is invited to call the undersigned directly.

Respectfully submitted,

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